

### **REMARKS**

Applicants respectfully request entry of the amendment and reconsideration of the outstanding rejections of the claims. Claims 1-5 have been canceled without prejudice. New claims 6-9 have been added. Accordingly, claims 6-9 are pending after entry of this amendment. Applicant submits that the new claims are supported throughout the specification and do not raise any issues of new matter.

#### **Petition for Extension of Time**

A three-month extension of time is requested extending the date for timely response to October 18, 2002.

#### **Rejection of Claims Under § 112, Second Paragraph**

The Examiner rejected claims 1-5 under 35 U.S.C. § 112, second paragraph. The Examiner objected to certain phrases used in the claims. Although this rejection has not been applied to the newly presented claims, it is discussed insofar as it might apply. Applicants respectfully traverse this rejection.

The newly presented claims do not include the phrases objected to by the Examiner.

Accordingly, Applicants submit that the newly presented claims fully comply with § 112, second paragraph, and withdrawal of this rejection is respectfully requested.

#### **Rejection of Claims Under § 102(b)**

The Examiner rejected claims 1-4 under 35 U.S.C. § 102(b) as anticipated by Lee et al. (Tubercle and Lung Disease, 78:12-19 (1997)). Although this rejection has not been applied to the newly presented claims, it is discussed insofar as it might apply. Applicants respectfully traverse this rejection.

The newly presented claims include the limitation of claim 5, which was not subject to this rejection. Thus, this rejection does not apply to the newly presented claims.

Accordingly, based on the foregoing differences, it is submitted that the reference cited in this rejection neither teaches nor suggests the presently claimed methods, and withdrawal of this rejection is respectfully requested.

### **Rejection of Claims Under § 103(a)**

The Examiner rejected claims 1-5 under 35 U.S.C. § 103(a) as being obvious over Lee et al. in view of Taylor (Methods in Molecular Biology, 70:273-278 (1997)). Although this rejection has not been applied to the newly presented claims, it is discussed insofar as it might apply. Applicants respectfully traverse this rejection.

The Examiner asserts that PCR primers comprising sequence of SEQ ID NO:3 and SEQ ID NO:4 would have been obvious to one skilled in the art based on a computer program. Applicants respectfully disagree.

The primary Lee et al. reference does not teach, suggest, or motivate a skilled worker to arrive at a method employing the specific primers recited in the claims.

The secondary Taylor reference does not remedy the shortcomings of the Lee et al. reference. Taylor is an inappropriate basis for a rejection under 35 U.S.C. § 103(a). Applicant's claims recite particular primers specific for REP13E12. In contrast, the software program called "GeneJockey II" merely generates possible proposed primer pairs for a target sequence. The fact the software program generates or could generate a given primer pair does not mean the primer pair is useful or effective because the software itself cannot prove the usefulness and effectiveness of generated primer pairs. Applicant could not use Taylor as an enabling basis for the rejected claims. It is therefore inappropriate for the Examiner to use the computer software as a basis for an obviousness rejection.

Unlike primer pairs that could be generated by computer software, the experiments described in Examples 1 to 7 of the present invention demonstrate that the primer pairs (SEQ ID: No. 3 and SEQ ID: No. 4) employed in the present invention detect *Mycobacterium tuberculosis* complex in clinical specimens by PCR. The REP13E12-PCR method of the present invention that uses primer pairs (SEQ ID: No. 3 and SEQ ID: No. 4) has been demonstrated to be more accurate in detecting *Mycobacterium tuberculosis* complex in clinical specimens than conventional diagnostic methods or IS6110-based PCR. See Table 2.

The Examiner asserts that Lee et al. teaches a method for detecting *Mycobacterium tuberculosis* using PCR amplification to amplify all or a portion of a 435 base pair repeat sequence. Although Lee et al. describes PCR amplification of a 453 base pair repeat sequence of *Mycobacterium tuberculosis*, the reference does not contain any concrete data that the 453 base pair repeat sequence is useful for PCR detection of *Mycobacterium tuberculosis* complex in

clinical specimens. For the 453 base pair repeat sequence to be useful for PCR detection of *Mycobacterium tuberculosis* in clinical specimens, testing such as that reported in the Examples in the present application must be carried out. Such tests employ a number of clinical specimens and compare results with conventional diagnosis methods and other PCR methods for identifying *Mycobacterium tuberculosis*. The document by Lee et al. neither contains such data nor describes any specific PCR primers designed and proved to be useful in detecting *Mycobacterium tuberculosis* in clinical specimens.

In contrast, the present application includes data demonstrating that REP13E12-PCR is useful for PCR detection of *Mycobacterium tuberculosis* complex in clinical specimens. The present examples report examination of 17 bacterial species, in addition to *Mycobacterium tuberculosis*, that can be present in clinical specimens from persons suspected of having tuberculosis. The data revealed that *Mycobacterium tuberculosis*-specific PCR amplification with Applicant's specific primer sets did not occur in bacterial species other than *Mycobacterium tuberculosis*. See Figure 3. The claimed method is specific to *Mycobacterium tuberculosis*.

Applicant's method requires employing the REP13E12 PCR primer sets and assaying for *Mycobacterium tuberculosis* in clinical specimens. Neither cited reference alone or in combination suggests such a method. Lee et al. does not teach a PCR method for detecting *Mycobacterium tuberculosis* in clinical specimens nor does the reference teach primers comprising sequence of SEQ ID NO:3 and SEQ ID NO:4. Taylor does not teach PCR primer sets comprising sequence of SEQ ID NO:3 and SEQ ID NO:4 nor does Taylor suggest that primer sets generated by the "GeneJockey II" software can be used to assay for *Mycobacterium tuberculosis* in clinical specimens.

Accordingly, based on the foregoing differences, it is submitted that the references cited in this rejection neither teach nor suggest the presently claimed methods, and withdrawal of this rejection is respectfully requested.

**Summary**

Claims 6-9 are in condition for allowance, and notification to that effect is earnestly solicited. The Examiner is invited to contact Applicant's representative if prosecution may be assisted thereby.

Respectfully submitted,

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